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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/690,855	10/22/2003	Henry Wolfe	NIDN-73175 DIV	6934

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AMERSHAM HEALTH  
IP DEPARTMENT  
101 CARNEGIE CENTER  
PRINCETON, NJ 08540-6231

EXAMINER

NAVARRO, ALBERT MARK

ART UNIT	PAPER NUMBER
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1645

DATE MAILED: 11/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 10/690,855	<b>Applicant(s)</b> WOLFE ET AL.	
	<b>Examiner</b> Mark Navarro	<b>Art Unit</b> 1645	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
  - If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
  - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
  - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-10 and 22-28 is/are pending in the application.  
     4a) Of the above claim(s) 23-28 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-7, 10 and 22 is/are rejected.
- 7) ☒ Claim(s) 8 and 9 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
     Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
     Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
     a) ☒ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. 09/914,162.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| <p>1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)</p> <p>2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)</p> <p>3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br/>             Paper No(s)/Mail Date <u>10/22/03</u>.</p> | <p>4) <input type="checkbox"/> Interview Summary (PTO-413)<br/>             Paper No(s)/Mail Date. ____.</p> <p>5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)</p> <p>6) <input type="checkbox"/> Other: ____.</p> |
|--|---|

## **DETAILED ACTION**

### ***Election/Restrictions***

Applicant's election without traverse of Group I, claims 1-10, and 22 in the reply filed on July 22, 2004 is acknowledged.

### ***Claim Rejections - 35 USC § 112***

1. Claim 2 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claim is vague and indefinite in the recitation of "mutated diphtheria toxin." One of skill in the art would be unable to determine the metes and bounds of the claimed invention. For instance what amount of modification is permitted to a diphtheria toxin to be considered a mutated toxin? Conversely at what point is the modification so great as to no longer be encompassed by the term "modified toxin?" Without a clear definition as to the term "modified diphtheria toxin" one of skill in the art would be unable to determine the metes and bounds of the claimed invention.

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

Art Unit: 1645

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 1-3, 5-7 and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by Rappuoli.

The claims are directed to a method for the production of diphtheria toxin wherein a microorganism capable of producing diphtheria toxin is fermented using glucose as a carbon source, said method comprising adding glucose to a growing culture whereby the addition of glucose maintains a microorganism growth effective to support diphtheria toxin production.

Rappuoli (US Patent Number 4,925,792) disclose of a method for the production of a mutated diphtheria toxin with a cytotoxic A subunit, wherein *Corynebacterium diphtheriae* is fermented comprising adding glucose to the growing culture. (See Columns 2 and 7). Rappuoli further disclose of a growth medium comprising cystine and maintaining the pH of the culture between 6.5 and 7.5. (See column 5).

3. Claims 1 and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by Gelfand et al.

The claims are directed to a method for the production of diphtheria toxin wherein a microorganism capable of producing diphtheria toxin is fermented using glucose as a carbon source, said method comprising adding glucose to a growing culture whereby the addition of glucose maintains a microorganism growth effective to support diphtheria toxin production, wherein the microorganism is *E. coli*.

Art Unit: 1645

Gelfand et al (US Patent Number 4,711,845) disclose of the production of diphtheria toxin fragments in *E. coli* strains. (See column 4 and Examples). Gelfand et al further disclose of adding glucose to the growing culture. (See column 16).

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 1-7, and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rappuoli in view of Johnson et al.

The claims are directed to a method for the production of diphtheria toxin wherein a microorganism capable of producing diphtheria toxin is fermented using glucose as a

Art Unit: 1645

carbon source, said method comprising adding glucose to a growing culture whereby the addition of glucose maintains a microorganism growth effective to support diphtheria toxin production, wherein the diphtheria toxin is CRM 107.

The teachings of Rappuoli are set forth above.

Rappuoli do not teach of producing the diphtheria toxin CRM 107.

Johnson et al (US Patent Number 5,728,383) teach of the diphtheria toxin CRM 107 and its usefulness in treating metastatic tumors of small cell lung carcinoma, when conjugated with an antibody. (See abstract and Column 18). Johnson et al further disclose of the nucleic acid sequence encoding CRM 107.

Given that 1) Rappuoli teach of a method for the production of diphtheria toxin comprising adding glucose to a growing culture of microorganisms, and that 2) Johnson et al have taught of the CRM 107 mutated diphtheria toxin and its ability to treat metastatic tumors, it would have been prima facie obvious to have incorporated the CRM 107 mutated diphtheria toxin as taught by Johnson et al in the method for production of diphtheria toxin comprising adding glucose to a growing culture of microorganisms as taught by Rappuoli. One would have been motivated to produce such a method based upon the teachings of Johnson et al that the CRM 107 mutated diphtheria toxin is capable of treating metastatic tumors.

***Specification***

The abstract of the disclosure is objected to because the abstract should not contain any legal phrases, e.g., "said." Correction is required. See MPEP § 608.01(b).

Claims 8 and 9 are objected to for depending upon a rejected base claim, however, claims 8-9 are free of the prior art of record.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark Navarro whose telephone number is (571) 272-0861.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Art Unit: 1645

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Mark Navarro  
Primary Examiner  
November 22, 2004